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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Tesfaye Zerihun Yigzaw

SERIAL NO: 09/442,256

GROUP ART UNIT: 1651

FILED: November 17, 1999

EXAMINER: Dr. H. Lilling

FOR: ANTI-CANCER PHARMACEUTICAL COMPOSITIONS AND METHODS



I hereby certify that this document, together with any document referred to as enclosed or attached, is being transmitted to the assistant commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, via first-class mail, on this 16<sup>th</sup> day of August, 2003.

*Tesfaye Yigzaw*

DATE: August 16, 2003

Assistant Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE UNDER 37 CFR 1.121

Sir:

Responsive to the Office action dated May 29, 2003, setting a shortened statutory period for response expiring on August 29, 2003, applicant respectfully submits the following remarks and amendments in connection with the above-identified application.

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- 1. (canceled) a composition comprising a therapeutically effective amount of an organic solvent extract of plant material, wherein said plant material is obtained from a plant selected from the group consisting of *Glinus lotoids*, *Ruta chalepensis*, *Hagenia abyssinica*, and *Millettia ferruginea*,--
- 2. (canceled) a composition comprising a therapeutically effective amount of one or more extracts of plant material is obtained from a plant selected from the group consisting of *Glinus lotoids*, *Ruta chalepensis*, *Hagenia abyssinica*, and *Millettia ferruginea*,--
- 3. (canceled) the composition of claim 2, where the extracts of plant material are obtained by contacting the plant material with a solvent selected from the group consisting of organic solvents, cell media, and water.--
- 4. (currently amended) the method, of claim 22, wherein the solvent selected from the group consisting of hexane, ether, and acetone or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone, is polar.--
- 5. (withdrawn ) the method of claim 22, wherein the solvent or mixture of solvents is non-polar.--
- 6. (previously amended) the method of claim 22, wherein the solvent is organic and is selected from the group consisting of methanol, hexane, ether, and acetone.--
- 7. (canceled) the composition of claim 3, wherein the cell media is selected from the group consisting of 10% DMEM, serumless DMEM, RPMI 1640, HAM's F12, CMRL 1066, McCoy's

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5A, Medium 199, Waymouth MB752, Eaglik MEM, and alpha-MEM.--

--8. (previously amended) the method of claim 22, wherein the plant material is selected from the group consisting of flowers, leaves, seeds, stems, and mixtures thereof.--

--9. (previously amended) the method of claim 22, wherein the composition comprises two or more extracts of plant material derived from the same or different plants.--

--10. (canceled) the composition of claim 2, further comprising a suitable pharmaceutical carrier.--

--11. (canceled) the composition of claim 10, wherein the pharmaceutical carrier is suitable for oral administration, intranasal administration, rectal administration, or parenteral administration.--

--12. (previously amended) the method of claim 40, wherein the parenteral administration is intravenous, subcutaneous, intramuscular, or intraperitoneal injection.--

--13. (previously amended) the method of claim 38, wherein the pharmaceutical carrier is in a form selected from the group consisting of tablets, capsules, powders, suppositories, suspensions, and solutions.--

--14. (previously amended) the method of claim 38, wherein the pharmaceutical carrier comprises coloring agents, flavoring agents, or combinations thereof.--

--15. (canceled) the composition of claim 2, wherein the extract of plant material is prepared in a form of liquid, powder, or tablet.--

--16. (cancelled) the composition of claim 2, wherein the extract of plant material is present in an

amount ranging 1 to about 100% by weight of the composition.--

--17. (canceled) the composition of claim 16, wherein the extract of plant material is present in an amount ranging from 10 to about 90% by weight of the composition.--

--18. (canceled) the composition of claim 17, wherein the extract of plant material is present in an amount ranging from about 20 to 80% by weight of the composition.--

--19. (canceled) the composition of claim 18, wherein the extract of plant material is present in an amount ranging from about 30 to 70% by weight of the composition.--

--20. (canceled) the composition of claim 19, wherein the extract of plant material is present in an amount ranging from about 40 to 60% by weight of the composition.--

--21. (canceled) the composition of claim 20, wherein the extract of plant material is present in an amount that is about 50% by weight of the composition.--

--22. (currently amended) a method for preparing the composition comprising one or more extracts of plant material, wherein the plant material is obtained from a plant selected from the group consisting of *Hagenia abyssinica* and *Millettia ferruginea*, comprising:

- (a) Contacting the plant material with a solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone, to form a liquid extract and a crude material, and
- (b) Separating the liquid extract from the crude material.

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--23. (canceled) the composition of claim 22, wherein the solvent comprises cell media or water, comprising:

(a) contacting the plant material with the cell media or water, the cell media or water present in amount sufficient to substantially cover the plant material.

(b) mixing the plant material and cell media or water to form a mixture, and

(c) separating the mixture into a liquid extract and a crude material.--

--24. (previously amended) the method of claim 22, wherein separating (b) comprises a method selected from the group consisting of centrifugation, filtration, and allowing the mixture to settle.--

--25. (previously amended) the method of claim 22, wherein separating (b) comprises multiple centrifugations resulting in the recovery of multiple liquid extracts.--

--26. (original) the method of claim 25, wherein the multiple liquid extracts are combined.--

--27. (canceled) the method of claim 23, wherein mixing (b) is accomplished by vortexing.--

--28. (canceled) the method of claim 22, wherein the solvent composition a first or a mixture of organic solvents, and wherein contacting the plant material with the first organic solvent or mixture of organic solvents forms a first liquid extract and a first crude material.--

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--29. (currently amended) the method of claim 22, further comprising:

(c) contacting the crude material one or more times with the same or different solvent

selected from the group consisting of hexane, ether, and acetone, or mixture of solvents

selected from the group consisting of methanol, hexane, ether, and acetone to form one or

more additional liquid extracts and one or more additional crude materials, and

(d) separating the one or more additional liquid extracts from the one or more additional crude materials.--

--30. (canceled) the method of claim 29, wherein the additional crude material is extracted one or more times using an organic solvent or a mixture of solvents to form further additional liquid extracts.--

--31. (canceled) the method of claim 29, wherein the first liquid extract is combined with the additional liquid extract.--

--32. (currently amended) the method of claim 29 , further comprising:

repeating (a) --(d) using a different plant material and the same or different solvent selected

from the group consisting of hexane, ether, and acetone, or a mixture of solvents selected

from the group consisting of methanol, hexane, ether, and acetone.

--33. (canceled) the method of claim 32, further comprising separating the second liquid extract from the second crude material and combining the first and second liquid extracts to form a mixture thereof.--

--34. (canceled) the method of claim 32, further comprising separating the second liquid extract and the second crude material, and again extracting the first or the second crude material one or more times using an organic solvents or a mixture of solvents, to form additional liquid extract.--

--35. (canceled) the method of claim 34, wherein the first and second extracts are combined with the additional liquid extracts.--

--36. (Previously amended) the method of claim 29, further comprising:

- (i) optionally combining one or more of the one or more liquid extracts;
- (ii) removing the solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents from the one or more liquid extracts to produce a substantially dried pellet, and
- (iii) suspending the substantially dried pellet in an aqueous solution.--

--37. (canceled) the method of claim 32, wherein the first and second organic solvents are removed from the solution of the first and second liquid extract to produce a substantially dried pellet, and wherein the substantially dried pellet is suspended in aqueous solution.--

--38: (original) the method of claim 22, further comprising combining the liquid extract with a suitable pharmaceutical carrier.--

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--39. (currently amended) the method of claim 22, further comprising:

(a) removing the solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone from the liquid extract to produce a substantially dried pellet, and

(b) combining the substantially dried pellet with a suitable pharmaceutical carrier.--

--40. (original) the method of claim 38, wherein the pharmaceutical carrier is suitable for administration by a method selected from the group consisting of oral administration, intranasal administration, rectal administration, and parenteral administration.--

--41. (cancelled) a method of treating breast cancer, prostate cancer, leukemia, melanoma, myeloma, HIV and other viral infection, diabetes, Parkinson's disease, tuberculosis, or fungal infections comprising administration a therapeutic amount of one or more extracts of plant material, wherein the plant is obtained from a plant selected from the group consisting of *Glinus lotoids*, *Ruta chalepensis*, *Hagenia abyssinica*, and *Millettia ferruginea* either alone or in combination with a suitable pharmaceutical composition, to a patient in need thereof,--

--42. (canceled) the method of claim 41, wherein the cancer is selected from the group consisting of breast cancer, leukemia, melanoma, and myeloma.--



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--43. (canceled) the method of claim 41, wherein the composition is administered by a method selected from the group consisting of oral administration, intranasal administration, rectal administration, and parenteral administration.--

--44. (canceled) the method of claim 43, wherein the parenteral administration comprises intravenous, subcutaneous, intramuscular, or intraperitoneal.--

--45. (canceled) the method of claim 43, wherein the amount of the composition administered per day ranges from about 5g/kg body weight of the patient.--

--46. (canceled) the method of claim 43, wherein *Millettia ferruginea* is administered orally at a daily dosage level ranging from about 10 mg/kg to about 100 mg/kg body weight of the patient.--

--47. (canceled) the method of claim 43, wherein *Millettia ferruginea* is administered intravenously at a daily dosage level ranging from about 5 mg/kg to about 20 mg/kg body weight of the patient.--

--48. (canceled) the method of claim 43, wherein *Hagenia abyssinica* is administered orally at a daily dosage level ranging from about 50 mg/kg to about 200 mg/kg body weight of the patient.--

--49. (canceled) the method of claim 43, wherein *Hagenia abyssinica* is administered intravenously at a daily dosage level ranging from about 10 mg/kg to about 50 mg/kg body weight of the patient.--

--50. (canceled) the method of claim 43, wherein *Ruta chalepensis* is administered orally at a daily dosage level ranging from about 10 mg/kg to about 2mg/kg body weight of the patient.--

--51. (canceled) the method of claim 43, wherein *Ruta chalepensis* is administered intravenously at a daily dosage level ranging from about 50 mg/kg to about 1000 mg/kg body weight of the patient.--

--52. (canceled) the method of claim 43, wherein *Glinus lotoides* is administered orally at a daily dosage level ranging from about 50 mg/kg to about 200 mg/kg body weight of the patient.--

--53. (canceled) the method of claim 43, wherein *Glinus lotoides* is administered intravenously at a daily dosage level ranging from about 10 mg/kg to about 50 mg/kg body weight of the patient.--

--54. (currently amended) a method for preparing a composition comprising one or more extracts of plant material, wherein the plant material is obtained from a plant selected from the group consisting of *Glinus lotoides*, *Ruta chalepensis*, *Hagenia abyssinica*, and *Millettia ferruginea*, comprising:

- (a) contacting the plant material with a solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents selected from the group consisting of

methanol, hexane, ether, and acetone to form a liquid extract and a crude material;

(b) separating the liquid extract from the crude material; and

(c) contacting the crude material one or more times with the same or

different solvent or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone to form one or more additional crude materials and one or more additional liquid extracts.--

--55. (currently amended) the method of claim 54, further comprising repeating (a) - (c) using a different plant material and the same or different solvent or a mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone.--

--56. (previously added) the method of claim 54, further comprising:

(i) optionally combining one or more of the one or more liquid extracts; and

(ii) mixing the one or more liquid extracts with a suitable pharmaceutical carrier.--

--57. (previously added) the method of claim 54, wherein the plant material comprises *Hagenia abyssinica* or *Millettia ferruginea* or both.--

--58. (currently amended) a method for preparing a composition comprising one or more extracts of plant material, wherein the plant material is obtained from a plant selected from the group

consisting of *Glinus lotoides*, *Ruta chalepensis*, *Hagenia abyssinica*, and *Millettia ferruginea*, comprising:

(a) contacting the plant material with a solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone to form a liquid extract and a crude material;

(b) separating the liquid extract and the crude material; and

(c) optionally contacting the crude material one or more times with the same or different solvent or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone to form one or more additional crude materials and one or more additional liquid extracts, wherein at least one of the contacting steps (a) or (c) comprises adjusting the pH by adding a basic compound or an acidic compound to form an adjusted mixture.--

--59. (previously added) the method of claim 58, wherein the pH is adjusted by adding a basic compound.--

--60. (previously added) the method of claim 59, wherein the basic compound is NaOH.--

--61. (previously added) the method of claim 59, wherein the pH is adjusted to a value between about 9 to about 13.--

--62. (previously added) the method of claim 58, wherein the pH is adjusted by adding an acidic

compound. --

--63. (previously added) the method of claim 62, wherein the acidic compound is HCl.--

--64. (currently amended) the method of claim 62, wherein ~~the~~ of the pH is adjusted to a value ~~between~~ from about 1 to about 5.--

--65. (previously added) the method of claim 58, further comprising re-adjusting the pH of the adjusted mixture, comprising:

- (i) adding an acidic compound if a basic compound was added, or
- (ii) adding a basic compound if an acidic compound was added.--

--66. (previously added) the method of claim 58, further comprising:

- (d) optionally combining one or more of the one or more liquid extracts;
- (e) adjusting the pH to about 6 to about 8; and
- (f) mixing the one or more liquid extracts with a suitable pharmaceutical carrier.--

--67. (currently amended) the method of claim 58, further comprising repeating (a) - (c) using a

different plant material and the same or different solvent or a mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone.--

--68. (previously added) the method of claim 58, wherein the plant material comprises *Hagenia abyssinica* or *Millettia ferruginea* or both.--

--69. (currently amended) a method for preparing a composition comprising one or more extracts of plant material, wherein the plant material is obtained from a plant selected from the group consisting of *Glinus lotoides*, *Ruta chalepensis*, *Hagenia abyssinica* and *Millettia ferruginea*, comprising:

(a) contacting the plant material with a solvent selected from the group consisting of hexane, ether, and acetone, or mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone to form a first liquid extract and a first crude material;

(b) separating the first liquid extract from the first crude material;

(c) contacting the first crude material with the same or a different solvents or a mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone comprising a second liquid extract and a second crude material;

(d) adjusting pH of the mixture (c) by adding a basic compound;

(e) separating the second liquid extract from the second crude material;

(f) contacting the second crude material with the same or a different solvents or a mixture of solvents selected from the group consisting of methanol, hexane, ether, and acetone to form a mixture comprising a third liquid extract and a third crude material;

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(g) adjusting the pH of the mixture (f) by adding an acidic compound; and

(h) separating the third liquid extract from the third crude material.--

--70. (previously added) the method of claim 69, further comprising:

(i) optionally performing additional contacting, adjusting, or separating steps;

(ii) combining one or more of the liquid extracts;

(iii) adjusting the pH to about 6 to about 8; and

(iv) mixing the one or more liquid extracts with a suitable pharmaceutical carrier.--

-- 71. (previously added) a composition obtained by the method of claim 22.--

-- 72. (previously added) a composition obtained by the method of claim 54.--